given to charge Deposit Account No. 23-17603 in the amount of Nine Hundred and Twenty Dollars ($920.00) to cover the extension fee as required by 37 C.F.R. §§1.17(a)(3) and 1.136(a).

IN THE CLAIMS:

Amend and substitute amended claim 19 for pending claim 19 as follows:

19. (Twice amended) A pharmaceutical composition comprising a therapeutically effective amount of the optically pure compound according claim 1 as active ingredient and a pharmaceutically acceptable carrier.

REMARKS

I. Lineage of Referenced Application

The referenced application is a continuation of U.S. Patent Application Serial No. 09/187,277, filed November 6, 1998, now abandoned (the "'277 application"), which is a continuation of U.S. Patent Application Serial No. 08/899,931, filed July 24, 1997, now abandoned, which is a continuation of U.S. Patent Application Serial No. 08/376,512, filed January 23, 1995, now U.S. Patent No. 5,714,504, issued February 3, 1998 (the "'504 patent"), which is a continuation-in-part of U.S. Patent Application Serial No. 08/256,174, filed June 28, 1994 as a 35 U.S.C. §371 application of PCT/SE94/00509, filed May 27, 1994, now U.S. Patent No. 5,693,818, issued December 2, 1997 (the "'818 patent").

II. Restriction Requirement

Restriction to one of the following inventions is required under 35 U.S.C. §121:

I. claims 1, 19, 21, 22 and 35, directed to an optical pure compound, classified in class 546, subclass 270+;

II. claims 36 and 37, drawn to an intermediate, classified in class546, subclass 270+; and

III. claims 8, 9 and 38-42, drawn to a process of preparing the compound of group I, classified in class 546, subclass 270+.

Applicants confirm the provisional election of the invention of Group I for prosecution purposes and withdraw the traversal of record. Notwithstanding this election, Applicants reserve the right to file one or more divisional applications directed to the claims of non-elected Groups II and III which are withdrawn from further consideration.

III. Description of Invention

Claim 1 is directed to an optically pure compound which is a magnesium salt of (-)-5-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole. Claim 35 is directed to the compound of claim 1 in its crystalline form. For ease of discussion in this Amendment, the generic name "omeprazole" will be used hereinafter for the compound 5-methoxy-2[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole.

Applicants have discovered that the magnesium salt of the (-)-enantiomer of omeprazole has an advantageous pharmacokinetic profile when compared, directly or indirectly, whatever the case may be, to omeprazole racemate and the magnesium salt of omeprazole racemate. Applicants submit that the different and more advantageous pharmacokinetic and pharmacodynamic properties of the claimed magnesium salt of (-)-omeprazole are neither

disclosed nor suggested in the prior art.

The Examiner's attention is kindly directed to the Declaration of Tommy Andersson which was submitted in the preceding '277 application. The comparative data presented in the Declaration of Tommy Andersson demonstrate that the claimed magnesium salt of the (-)-enantiomer of omeprazole exhibits pharmacokinetic advantages when compared, directly or indirectly, whatever the case may be, to clinical results obtained with the racemic form of omeprazole or the magnesium salt of the racemic form of omeprazole by virtue of higher dose efficiency and significantly less interindividual variation. Accordingly, the claimed invention represents a patentable advancement over the prior art.

IV. The Office Action

Claims 1, 19, 21, 22 and 35 are rejected for the following reasons:

1. under 35 U.S.C. §103(a) as being anticipated by U.S. Patent No. 4,738, 974 to Brändström (the "'974 patent) and by DE 4,035,455 ("DE '455");
2. under 35 U.S.C. §101 as claiming the same invention as that of prior U.S. Patent No. 5,900,424 to Källström et al. (the "'424 patent"); and
3. under the judicially created doctrine of obviousness-type double patenting over claims of Applicants' co-pending U.S. Patent Application Serial No. 09/077,719 (the "'719 application").

Additionally, claims 19, 21 and 22 are rejected under the judicially created doctrine of obviousness-type double patenting over claims of the '974 and '504 patents and U.S. Patent No. 5,817,192 to Lindberg et al. (the "'192 patent") . Claim 19 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which allegedly was not described in the specification in

such a way as to enable one skilled in the art to make and/or use the invention.

V. Claim Rejections - 35 U.S.C. §103(a)

Claims 1, 19, 21, 22 and 35 are rejected under 35 U.S.C. §103(a) as being unpatentable over the '974 patent and DE '455.

In the preceding '277 application, the corresponding claims were rejected under 35 U.S.C. §102(b) for lack of novelty in view of the same prior art. However, the §102 rejection of record has been withdrawn. Applicants submit that the withdrawal of the §102 rejection is an acknowledgment that the claimed invention is not identically disclosed or described in the prior art.

Therefore, the issue is whether the claimed invention would have been obvious to the person of ordinary skill in the art at the time the invention was made. It is well established that the determination of obviousness under 35 U.S.C. §103 involves factual inquiries including secondary considerations such as "unexpected results".

The results of the clinical studies as reported in the Declaration of Tommy Andersson confirm that the claimed (-)-enantiomer of omeprazole is defined by a different and more advantageous pharmacokinetic profile in comparison, either directly or indirectly, whatever the case may be, to either the racemic form of omeprazole or the magnesium salt of omeprazole. The therapeutic profile of the claimed invention includes a number of important advantages such as a higher dose efficiency, less interindividual variation in AUC and longer duration of elevated intra-gastric pH. It is precisely this type of "greater than expected result" which has long been an evidentiary factor pertinent to a finding on nonobviousness (*United States v. Adams*, 383 U.S. 39,

51-52 (1966)).

Neither the '974 patent nor the DE '455 reference teach or suggest the advantageous and distinguishing properties which characterize the claimed magnesium salt of the (-)-enantiomer of omeprazole. For all of the foregoing reasons, withdrawal of the rejections under 35 U.S.C. §103(a) is requested.

VI. Claim Rejection - 35 U.S.C. §101

Claims 1, 19, 21, 22 and 35 are rejected under 35 U.S.C. §101 as claiming the same invention as that of claims of the '424 patent. The rejection is moot as to claims 19, 21 and 22 since these claims have been canceled.

The term "same invention", as contemplated by 35 U.S.C. §101, means an invention drawn to identical subject matter. *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985). The test is whether the claims of the application and cited patent cover the same thing. *Carman Induc., Inc. V. Wahl*, 724 F.2d 932, 220 U.S.P.Q. 481 (Fed. Cir. 1983). For the following reasons, there is no identity of invention between claims 1, 19, 21, 22 and 35 of the claimed invention and the claims of the '424 patent. Rather, Applicants respectfully submit that the issue of double patenting is more properly addressed under the context of obviousness-type double patenting.

Claim 1 of the '424 patent defines a magnesium salt of omeprazole racemate having a degree of crystallinity which is higher than 70% as determined by x-ray powder diffraction. In contrast, the claimed compound is directed to the magnesium salt of the (-)-enantiomer of omeprazole. Applicants submit that the claims of the cited '424 patent and claims 1, 19, 21, 22 and 35 of the subject application do not cover the same compound and, therefore, they are not

used to encompass

directed to the same invention.

Omeprazole racemate consists of equal shares of its (+)- and (-)-isomers and the racemic mixture is defined by a set of physical and chemical properties. Similarly, the (-)-enantiomer of omeprazole is characterized by its own set of properties. As demonstrated by the Declaration of Andersson, the pharmacokinetic profile of (-)-omeprazole is distinguishable from that of the racemate. The different pharmacokinetic and metabolic profile relative to the (-)-enantiomer and racemate, respectively, suggests a lack of identity as required by 35 U.S.C. §101. Even if for the sake of argument, the (-)-enantiomer of omeprazole is considered to be a part of omeprazole, there is still a lack of identity since the (-)-enantiomer is a new chemical entity vis-à-vis the compound of the '424 patent.

Therefore, the double patenting rejection based on the '424 patent is improper and should be withdrawn. If the Examiner withdraws the double patenting rejection and issues an obviousness-type double patenting rejection in connection with the '424 patent, Applicants are prepared to file a Terminal Disclaimer under 35 U.S.C. §253.

VII. Claim Rejection - Obviousness-Type Double Patenting

Claims 1, 19, 21, 22 and 35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting rejection as being unpatentable over claims of the co-pending '719 application. The rejection is provisional because the conflicting claims have not in fact been patented. Accordingly, Applicants will comment or take appropriate action when the conflicting claims have in fact been patented and the rejection is no longer provisional.

Claims 19, 21 and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of the '974, '192 and '504 patents. It is

alleged that claimed invention that is not patentably distinct from claims of the '974, '192 and '504 patents.

As discussed in Section I, above, the subject application belongs to the same patent family as the cited '192 and '504 patents. Therefore, Applicants agree to submit a Terminal Disclaimer with respect to the '192 and '504 patents at such time when the remaining issues regarding patentability of the claimed invention have been resolved.

With specific regard to the '974 patent, Applicants respectfully submit that the obviousness-type double patenting rejection is contrary to the guidelines set forth in M.P.E.P. §804(II)(B)(1). An obviousness-type double patenting rejection is appropriate when any claim in the application defines an invention that is ***merely an obvious variation*** of an invention claimed in the patent. An obviousness-type double patenting rejection is analogous to the nonobviousness requirement of 35 U.S.C. §103. As such, the analysis employed in an obviousness-type double patenting determination must be based on the factual inquiries set forth in *Graham v. John Deere Co., 383 U.S. 1, 148 U.S.P.Q.4589 (1966).* Therefore, the Examiner is required to consider any objective indicia of nonobviousness, such as unexpected results.

Applicants submit that the comparative data set forth in the Declaration of Tommy Andersson obviates the obviousness-type double patenting rejection. Specifically, as shown in the Declaration of Tommy Andersson, the claimed (-)-enantiomer of omeprazole is defined by a different and more advantageous pharmacokinetic profile when compared either directly or indirectly, whatever the case may be, to either the racemic form of omeprazole or the magnesium salt of omeprazole. The therapeutic profile of the claimed invention includes a number of important advantages such as a higher dose efficiency, less interindividual variation in AUC and longer duration of elevated intra-gastric pH. In view of the evidence of unexpected results, the

claimed invention is more than just an obvious variation of the cited prior art. Withdrawal of the obviousness-type double patenting rejection based on the '974 patent is requested.

VIII. Claim Rejection - 35 U.S.C. §112

Claim 19 is rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which allegedly was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Claim 19 has been amended to recite a therapeutically effective amount of the active ingredient. Withdrawal of the rejection is requested.

Version showing additions to amended claim 19:

19. (Twice amended) A pharmaceutical composition comprising a therapeutically effective amount of the optically pure compound according claim 1 as active ingredient and a pharmaceutically acceptable carrier.

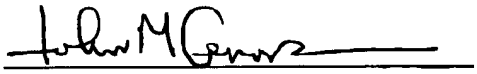
CONCLUSION

Claims 1, 19, 21, 21 and 35 are directed to patentable subject matter. Accordingly, Applicants request reconsideration and allowance of the claims.

Any additional fee due in connection with this response should be charged to Deposit Account No. 23-1703.

Dated: November 7, 2001

Respectfully submitted,



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